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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/376,430	08/18/99	MOORE	P PF466P1

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EXAMINER	
O HARA, E	
ART UNIT	**PAPER NUMBER**
1646	15

DATE MAILED: 03/26/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/376,430	Moore et al.
Examiner	**Group Art Unit**
Eileen B. O'Hara	1646

☒ Responsive to communication(s) filed on *01 Janurary 2001*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *24-101* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *24-101* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *13*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. Claims 24-101 are pending in the instant application. Claims 38, 39 and 40 have been amended and claims 1, 13, 17-19, 22 and 23 have been canceled as requested by Applicant in Paper Number 14, filed Jan. 5, 2001.

Withdrawn Rejections

2.1 The rejections of claims under 112 § 2 are withdrawn in view of Applicant's amendment.

2.2 The rejection of claims under 112 § 1 for the biological deposit is withdrawn in view of Applicant's statement on pages 7-8 of the amendment which serves to perfect the required deposit.

2.3 The rejection of claims under 35 USC § 102(b) is withdrawn in view of Applicant's amendment.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 24-101 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled

in the art to which it pertains, or with which it is most nearly connected, to use the invention, for reasons cited in the previous Office Action, Paper No. 11, at pages 3-6.

Claims 24-101 encompass a putative receptor molecule of the interleukin common gamma chain family, identified as Cytokine Receptor Common Gamma Chain Like or CRCGCL protein, based on homology to the cytokine receptor family and other common gamma chains. The reasons for the enablement rejection were discussed in the prior Office Action. Applicants traverse the rejection and argue that it would not require undue experimentation to use the invention. Applicants cite *Fields v. Conover* and state that "Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the art", indicating that this is the definition of "undue experimentation". However, *Fields v. Conover* actually state that "Disclosure complies with how-to-make requirement of 35 U.S.C. 112 even though some experimentation, provided it is not an undue amount and provided that it does not require ingenuity beyond that to be expected of one of ordinary skill in the art, is required to adapt invention to particular settings.", which is different from Applicants implied definition of "undue experimentation" because no use has been disclosed which can be "adapted". Rather, the issue here is that there is no enabled use. Applicants further present *In re Wands* for the factors used to determine undue experimentation, among which are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and the level of skill in the art, and state that the "test for undue experimentation is not merely quantitative, since a considerable

amount of experimentation is permissible, if it is merely routine.". In the case of *In re Wands,* the Federal Circuit found that the disclosure satisfied the requirements under 112 first paragraph, which disclosed one deposited antibody and claimed methods of using the genus of antibodies to a particular protein in an immunoassay. The Examiner in the case had rejected claims over antibodies because **making** the antibodies would be unpredictable and unreliable, so that it would require undue experimentation for one skilled in the art to make the antibodies. The court decided that making and using the antibodies would not require undue experimentation, and based its decision on the fact that the invention could be practiced with readily available starting materials using methods that are well known in the monoclonal antibody art, and because practitioners of the art are prepared to screen negative hybridomas in order to find one that makes the desired antibody. However, that situation is not comparable to the present situation. The enablement rejection was based on the disclosure providing adequate guidance in **making** antibodies, and in that particular case there was disclosed a working example (a specific antibody). In the present case, the enablement rejection is not based on the making of the CRCGCL protein or variants of the protein, but on the disclosure enabling the **use** of the protein(s). Given the level of skill in the art, if the specific biological activity of the protein were known, it would not require undue experimentation to determine how to use it, however there is no specific biological activity known for this protein. Applicants submit on page 5 of the amendment that since the disclosed or otherwise known methods of making and screening the claimed polypeptides may be used to determine, without undue experimentation, whether a given

polypeptide encompassed by the claims functions, for example, as a cytokine receptor, or in activating the Jaks-STAT signal transduction pathway, or in regulating the differentiation and/or proliferation of cells, or to routinely generate CRCGCL specific antibodies which could be used as immunological probes for differential identification of tissues or cells types, the enablement requirement is fully satisfied.

Applicant's arguments for the enablement of the protein have been considered but are not found persuasive. The specification does teach using the CRCGCL protein to make antibodies or use as probes for differential identification of tissues or cells, however these are not considered specific or substantial utilities for the protein, and hence are not enabling. Applicants are directed to the new utility examination guidelines published in the Federal Register, January 5, 2001, pages 1092-1099 (Volume 66, No. 4). Any protein can be used to generate antibodies to it, which can then be used as probes for the tissues that express it. The enablement rejection is based on assertions of using the protein as a "cytokine receptor", which is not a specific use, or in the general use of regulating the differentiation and/or proliferation of cells. Cytokine receptors are a large family of proteins that have diverse tissue expression, ligand specificity, and biological activities, and each receptor responds to different ligands, mediates different signals and produces different responses in different cell types. The protein is not enabled for use because it is not known what specific ligand binds to it, the specific signal generated and the specific cellular response that results, which is different from the other cytokine receptors, so one of skill in the art would not know how to use it.

There is considerable direction and guidance in the specification with respect to how to determine what the activity or function of the CRCGCL protein is. However, this is distinct from direction and guidance sufficient for one of skill in the art to **use** the invention. The test for enablement pertains to the determination of undue experimentation is needed to **practice** the invention. Without any such teachings it is an invitation to experiment. What Applicant has provided is a mere wish or plan and an invitation to experiment to determine what use the protein may have.

On pages 4-6 of the amendment, Applicants submit that the proper inquiry is not whether the specification teaches how to make and use all of the polypeptides encompassed by the claims, but rather, whether polypeptides encompassed by the claims have at least a single use, and cite *In re Vaeck, Ex parte Mark and In re Angstadt*. The issue in *Ex parte Mark* was enablement of cysteine-depleted muteins of biologically active proteins, which requires the muteins to retain biological function. In this case, the biological activities of the proteins were known, so it would not have required undue experimentation to screen for those muteins which would retain function and those which would not. This differs from the present situation, in which there is no known specific activity for the CRCGCL protein. If one of skill in the art knew how to use the CRCGCL protein and could screen for an activity or function, it would not be undue experimentation to screen variants of the CRCGCL protein. However, there is no known activity or function for the protein.

On page 6 of the amendment, Applicants state "Further, as Judge Rich explained in *In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q2d 1438, 1445 (Fed.Cir. 1991), the statutory enablement requirement is satisfied if the specification "adequately guides the worker to *determine,* without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility" (emphasis provided)." In this case the invention was directed to the use of genetic engineering techniques for production of proteins (*Bacillus* endotoxins) that are toxic to insects such as larvae of mosquitos and black flies by production of a chimeric gene *Bacillus* endotoxin gene into host cyanobacterium. The enablement rejection was based on the facts that the cyanobacteria comprise a large and diverse group of photosynthetic bacteria including large numbers of species in some 150 different genera, the molecular biology of these organisms had only recently become the subject of intensive investigation and this work was limited to a few genera, and the disclosure had only one working example in a single strain of cyanobacteria. However, the present situation differs from that of *In re Vaeck*, because there is no enabled use for the protein.

On pages 6 and 7 of the amendment, Applicants submit that the claimed polypeptides which share 90-95% identity with SEQ ID NO: 2 would be particularly useful, for example, in epitope-mapping, in generating CRCGCL specific antibodies which could be used as immunological probes for differential identification of tissues or in immunoassays to detect the polypeptides of the present invention. However, polypeptides which share 90-95% identity with SEQ ID NO: 2 would produce antibodies that would not be as specific as antibodies to the

protein of SEQ ID NO: 2, and therefore not as useful for these purposes. Additionally, as discussed above, these uses are not considered specific or substantial utilities for the protein.

On pages 7 and 8 of the amendment, Applicants submit that the Bowie reference is adequate in giving one skilled in the art guidance concerning which amino acid changes are phenotypically silent. Applicants also provide guidance in the specification of conservative and nonconservative amino acid replacements, and Applicants submit that the specification discloses the reference Cunningham and Wells, which teaches how to determine which amino acids of a protein are essential to its function, and assert that these disclosures are sufficient to enable one skilled in the art to make amino acid changes in up to 10% of the total number without changing the utility of the polypeptide. These disclosures would be enabling if one of skill in the art knew how to use the protein and assay for activity, but until the protein can be assayed for function, the effect of any amino acid changes cannot be determined.

As discussed in the previous Office Action, the factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (FED. Cir. 1988). As stated in the MPEP, 2164.01(a), "The examiner's analysis must consider all the evidence related to each of these factors, and any

conclusion of nonenablement must be based on the evidence as a whole. 858 F.2d at 737, 740, 8 USPQ2d at 1404, 1407." "The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404."

In the present case, there is not a single working example of any kind of activity, it is not predictable from sequence homology what the activity of the protein would be, and there is limited guidance on how to use the protein. The instant claims are drawn to a protein which has undetermined function or biological significance. This further characterization of the protein, is part of the act of invention, and until it has been undertaken the Applicant's claimed invention is incomplete. What Applicant has provided is a mere wish or plan and an invitation to experiment.

Therefore, the rejection of claims 24-101 under 35 U.S.C. 112, first paragraph, for lack of enablement, and for scope of enablement for polypeptides that are 90-95% identical to the polypeptides disclosed in the specification, is maintained.

It is believed that all pertinent arguments have been answered.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D

Patent Examiner

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER